REMARKS

The Amendment, filed in response to the Office Action mailed February 25, 2010, is believed to fully address all and every issue raised in the Office Action. Favorable reconsideration and allowance of the application are respectfully requested.

Claims Status and Amendment Summary

Claims 1-6, 8, 9, 11-13, 15 and 16 are all the claims pending in the application. Claim 15 is withdrawn from consideration.

In the instant amendment, claim 1 is amended to more clearly set forth the claimed subject matter. Amended claim 1 is supported by the disclosure of the specification, for example, at the paragraph bridging pages 26-27 of the specification (paragraph [0059] in application Publication No. 20060276633), the first full paragraph on page 47 of the specification (paragraph [0085] in application Publication No. 20060276633), and page 17, line 4 - page 18, line 7 of the specification (paragraph [0040] in application Publication No. 20060276633).

In the instant amendment, claims 2 and 3 are amended in order to set forth the Markush group in a more proper format.

In the instant amendment, claim 13 is amended to rewrite it in an independent claim format.

No new matter is introduced. Entry and consideration of the amendment are respectfully requested.

Response to Rejection Under 35 U.S.C. § 103

In the Office Action, the rejection of claims 1-6, 8 and 16 under 35 U.S.C. § 103 as being unpatetable over Kitai et al (Appl. Microbiol. Biotechno. 28(1):52-56) in view of Simmons et al. (Nat. Biotech. 14:629-34) and further in view of Sytkowski et al. (WO 99/02709) is maintained.

In the Office Action, the rejection of claims 1, 9 and 12 under 35 U.S.C. § 103 as being unpatetable over Kitai in view of Simmons, further in view of Sytkowski, and further in view of Lilly (US 20040053370) is maintained.

In the Office Action, the rejection of claims 1 and 11 under 35 U.S.C. § 103 as being unpatetable over Kitai in view of Simmons, further in view of Sytkowski, and further in view of Kwon et al. (WO200015661) is maintained.

In the Office Action, claims 1-6, 8 and 16 are rejected under 35 U.S.C. § 103 as being unpatentable over Andrews et al. (Gene 182:101-109 (1996)) in view of Simmons and further in view of Sytkowski.

Applicant respectfully disagrees.

Currently amended claim 1 recites

> A method of producing an immunoglobulin constant region, comprising:
> transforming *E. Coli* with a recombinant expression vector including a nucleotide sequence encoding an E.coli signal sequence ~~isolated from *E. Coli*~~ and a nucleotide sequence encoding an immunoglobulin constant region, without a variable region;

culturing a resulting transformant in a medium to overexpress the immunoglobulin constant region in the cytoplasm of the transformant, wherein the signal sequence of the overexpressed immnunoglobulin constant region is processed; and

isolating the immunoglobulin constant region expressed by the transformant,

wherein the signal sequence is a heat-stable enterotoxin II signal sequence, and wherein the immunoglobulin constant region is expressed in the cytoplasm in a water soluble form and is not secreted into the medium or the periplasmic space.

A technical feature of the present invention is in that a signal sequence is precisely and accurately processed (cleaved) in the cytoplasm so that the immunoglobulin constant region is overexpressed as a mature form, which is clearly shown through an N-terminal sequence analysis in Example 4. Also, in the general description of the invention, for example on page 17, line 4 - page 18, line 7 (paragraph [0040] of the published application), Applicant describes the "signal sequence' and "it processing" in a transformant.

First, none of the cited references teach the limitations "overexpress the immunoglobulin constant region in the cytoplasm of the transformant, wherein the signal sequence of the overexpressed immnunoglobulin constant region is processed" and "expressed in the cytoplasm in soluble form" of currently amended claim 1.

For example, the newly cited reference, Andrew, discloses that a target protein combined with the STII signal sequence is expressed in the cytoplasm. However, the target protein in Andrew is expressed in insoluble form (page 106, right column). Therefore, Andrew, either alone or in combination with Simmons, fails to teach all and every limitation of currently amended claim 1.

Also, the non-secreting constructs described in Simmons is produced as a precursor form, not as a mature form (p632, right handed column), and is thereby distinguished from the present invention.

Therefore, the combined teachings of cited references fail to teach all and every element of currently amended claim 1.

Furthermore, the Examiner fails to establish prima facie obviousness. That is, none of the cited references provide any guidance or teachings to modify their combined teachings to reach, with reasonable expectation of success, the claimed method, in particular, (a) "overexpressing the immunoglobulin constant region in the cytoplasm of the transformant, wherein the signal sequence of the overexpressed immnunoglobulin constant region is processed; and (b) "the constant region is expressed in the cytoplasm alone in a water soluble form."

In light of widely-recognized and well-accepted high unpredictability of the technology of interest, Applicant respectfully submits that the combination of the STII signal sequence (among numerous leading sequences) and an Fc region (among numerous target proteins) is not obvious. In particular, such is true, when considering the facts that expression efficiency of the target proteins in a fusion protein varies greatly from one protein to another protein. Furthermore, it is more difficult and unpredictable to produce a target protein in a soluble form in the cytoplasm of E. coli.

Therefore, Applicant respectfully, but strongly submit the rejections under 35 U.S.C. § 103 cannot be sustained and their withdrawal is respectfully requested.

Response to Rejection under 35 U.S.C. § 112, Written Description

In the Office Action, claims 1-6, 8, 9, 11-13 and 16 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner asserts that the specification teaches that the proteins are not secreted into the medium or the periplasmic space, but the previously amended claims only excludes the medium.

In response, without conceding the rejection, solely for the interests of Applicant to compact the prosecution, Applicant amends claim 1 to recite that the expressed protein is not secreted into the medium or the periplasmic space, rendering the rejection moot.

Therefore, withdrawal of the rejection under 35 U.S.C. § 112 is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number **202-775-7588**.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Sunhee Lee/

Sunhee Lee
Registration No. 53,892

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
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